Remarks

Amendments

Claims 29 and 38 have been amended as described below. Claim 34 has been cancelled. Claims 29, 33 and 35-41 are currently pending in the application.

The amendments to the claims have been made without prejudice and without acquiescing to any of the Examiner's objections. Applicant reserves the right to pursue any of the deleted subject matter in a further divisional, continuation or continuation-in-part application. No new matter has been entered by the present amendment and its entry is respectfully requested.

It is believed that the amendments and the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Should the Examiner deem it beneficial to discuss the application in greater detail, she is kindly requested to contact the undersigned by telephone at her convenience.

Rejection Under 35 USC §112, First Paragraph

Claims 29 and 33-41 were rejected under 35 USC §112, first paragraph as allegedly failing to comply with the enablement requirement. Applicant respectfully traverses this rejection as applied to the amended claims.

Specifically, the Examiner alleged that the "specification fails to enable one in the art to practice the method for preventing any of the claimed conditions. Prevention of a disease or condition requires a significant showing that the disease or condition is actually prevented". This is clearly not required under 35 U.S.C. 112, and the undersigned is aware of no case law or rule requiring such a showing. However, merely to facilitate allowance and without prejudice,

claim 29 has been amended in order to remove the phrase "or preventing" which overcomes the objection.

Rejection Under 35 USC §112, Second Paragraph

Claims 29 and 33-41 were rejected under 35 USC §112, second paragraph, as allegedly being indefinite. Applicant respectfully traverses this rejection.

Solely to facilitate allowance, and with the understanding that "an effective amount" to treat pancreatic damage is readily determinable by one of ordinary skill in the art, in compliance with decades of court decisions finding such terms definite, claim 29 has been amended in order to remove the phrase "an effective amount of", which overcomes the objection.

The Examiner alleged that claims 37 and 41 are vague and indefinite as it is unclear if the claims intend the method to further treat diabetes and hyperglycemia. As the Examiner noted, claim 29 from which these claims depend, relates to a method of treating pancreatic damage. Claims 38 and 41 further specify that the method also treats diabetes or hyperglycemia. It is known that pancreatic damage can lead to diabetes or hyperglycemia. In addition, pancreatic damage can also be product of diabetes or hyperglycemia. As a result, the cells can be used to treat diabetes and hyperglycemia in addition to treating pancreatic damage. The claims are not indefinite in this regard.

The Examiner rejected claim 38 as being indefinite for reciting "insulin dependent Type II diabetes". In response, this phrase has been amended to read non-insulin dependent Type II diabetes".

Rejection Under 35 USC §103

Claims 29, 33-34, 36-39 and 41 were rejected under 35 USC §103(a) as obvious over U.S. Published Application No. 2003/0082155 by Habner et al. ("Habner"). Claims 29, 33-35, 37-38 and 41 were rejected under 35 USC §103(a) as obvious over Ikehara et al. Proc. Natl. Acad. Sci, 82:7743-47 (1985) ("Ikehara"). Applicant respectfully traverses these rejections as applied to the amended claims

The Legal Standard

The starting point for any such analysis must be the Supreme Court's decision in *KSR,* which refocuses the determination of whether a claimed invention is obvious back to the process the Court had defined in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18 (1966). There, the Court had held that the obviousness determination should address four factors, all of which must be considered, though not in any prescribed order: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) any secondary considerations suggesting nonobviousness, such as commercial success, failure of others, and long felt but unmet need. *Id.* The Court cautioned that the fact finder should be careful about reading the teachings of the invention at issue into the prior art, to avoid applying inappropriate hindsight, *ex post* reasoning. *Id.* at 36.

In the chemical arts, where compounds are so similar as to create an expectation that the claimed new compound would have similar properties as the prior art compounds, the Federal Circuit also has upheld a finding that the claimed invention is not patentable. *Aventis Pharma Deutschland GmbH v. Lupin, Ltd.*, 499 F.3d 1293, 1301 (Fed. Cir. 2007). However, when the prior art disclosed a broad selection of compounds that might have been potential candidates for

further investigation, the lack of sufficient guidance and predictability to select the compound at issue supported a finding of nonobviousness. *Takeda Chem. Indus. Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1359-60 (Fed. Cir. 2007), *petition for cert. filed*, 76 U.S.L.W. 3374 (U.S. Dec. 20, 2007) (No. 07-838); *see also In re Sullivan*, 498 F.3d 1345 (Fed. Cir. 2007) (remanding to the Board, noting that despite close similarity of the claimed invention and prior art, rebuttal evidence to which the Board gave inadequate consideration showed unexpected results, a teaching away from appellant's invention and a long felt but unmet need).

Even where the prior art suggests or motivates an inventor to develop the composition or process at issue, the Federal Circuit continues to recognize that there is a critical question under 35 U.S.C. § 103 as to whether the combined teachings of the prior art "would have given rise to a reasonable expectation of success" in achieving what is claimed. *PharmaStem Therapeutics, Inc. v. ViaCell, Inc.*, 491 F.3d 1342, 1360 (Fed. Cir. 2007), *petition for cert. filed*, 76 U.S.L.W. 3393 (U.S. Jan. 2, 2008) (No. 07-888). There, the inventors merely used routine research methods to prove what was already believed to be the case and had not made a patentable invention. *Id.* at 1363-64. However, the court noted that a different case is presented if all the prior art suggested was to explore a general approach and gave only general guidance as to the particular form of the claimed invention or how to achieve it. *Id.* at 1364-65 (citing *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988), and *Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1166-67 (Fed. Cir. 2006), as continuing to provide useful guidance in determining whether the expectation of success from a line of inquiry found in prior art is so great as to make a resulting invention obvious).

Analysis

Claim 29 has been amended in order to specify that the regeneration initiating cell has the cell surface marker c-kit as well as at least one of CD34 and AC133 (CD133).

Claims 29, 33-34, 36-39 and 41 in view of Habner

Habner et al. describes the use of pancreatic stem cells for the treatment of Type I insulin-dependent diabetes. The stem cells described in Habner et al. are different from the claimed regeneration initiating cells. Habner et al. specifically exclude hematopoietic derived stem cell markers such as CD34 and CD133. They specifically state that bone marrow derived $CD34^+$ cells are not stem cell-like enough and distinguish the more pluripotent $CD34^-$ bone marrow derived population. In contrast, the claimed regeneration initiating cells (RICS) express endothelial cell markers and directly express at least one of two such hematopoietic markers ($CD34^+$ and/or AC133/CD133). Similarly, upon transplantation they do not demonstrate pluripotency along the pancreatic lineage including islets or Beta cells, but instead retain endothelial markers. Further, Habner et al. specifically target those endogenous stem cells that differentiate into insulin producing cells, not those that would differentiate/retain endothelial features to promote the endogenous regeneration of the pancreas to produce islets. RICS do not become islets. RICS represent distinct cells from the cells described in Habner et al., they are from distinct sources and have distinct outcomes (repair/regeneration vs direct replacement).

There is nothing in Habner et al. that would lead one of skill in the art to use regeneration initiating cells that are c-kit^+ and $CD34^+$ and/or $CD133^+$ cells to stimulate the regeneration or repair of damaged islet cells.

Claims 29, 33-35, 37-38 and 41 under 35 USC §103(a) in view of Ikehara

Ikehara et al. relates to a method of preventing Type I diabetes through transplantation of allogeneic bone marrow. The amended claims do not encompass "prevention" of diabetes. The method of Ikehara et al. represents a replacement of immune system (method of inducing immune tolerance) by mismatching the pancreatic cells to the immune cells in a clearly autoimmune based type I diabetes islet damage. This is demonstrated (pg 7747) wherein they indicate that they had "thus far not been able to treat diabetes that is already advanced in NOD mice" presumably by virtue of mice having lost islet cells. This indicates that that while bone marrow was transplanted, there was neither engraftment in the pancreas nor islet repair – just immune avoidance.

There is no predictability from Ikehara et al. to use the regeneration initiating cells as claimed in the present application to treat pancreatic damage by stimulating the regeneration or repair of damaged islet cells.

Allowance of claims 29, 33 and 35-41 as amended is earnestly solicited.

Respectfully submitted,

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